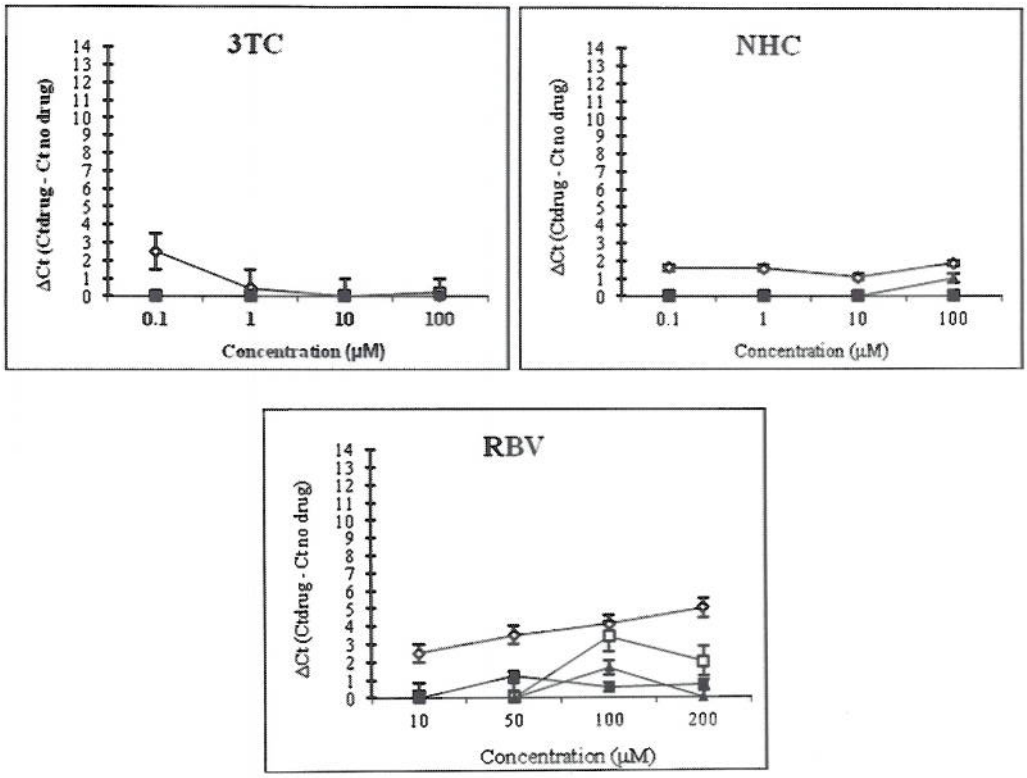
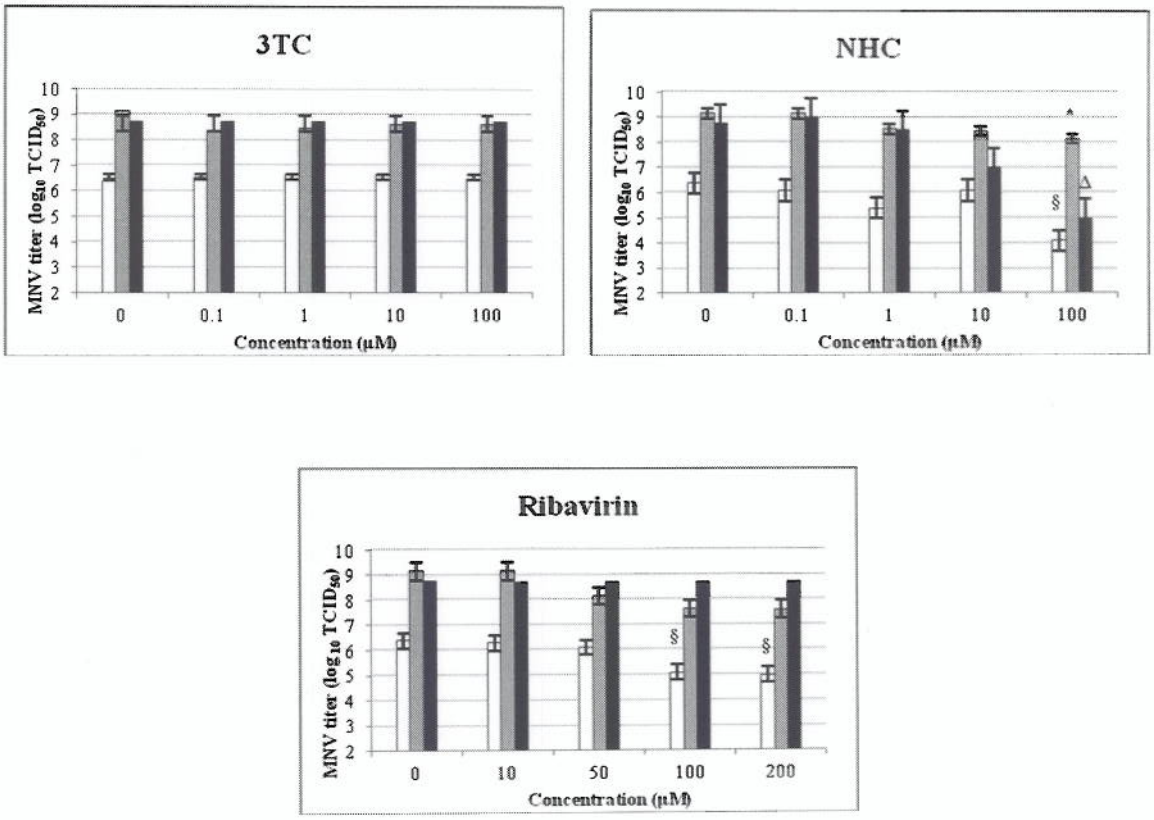
Supplemental Figure 1



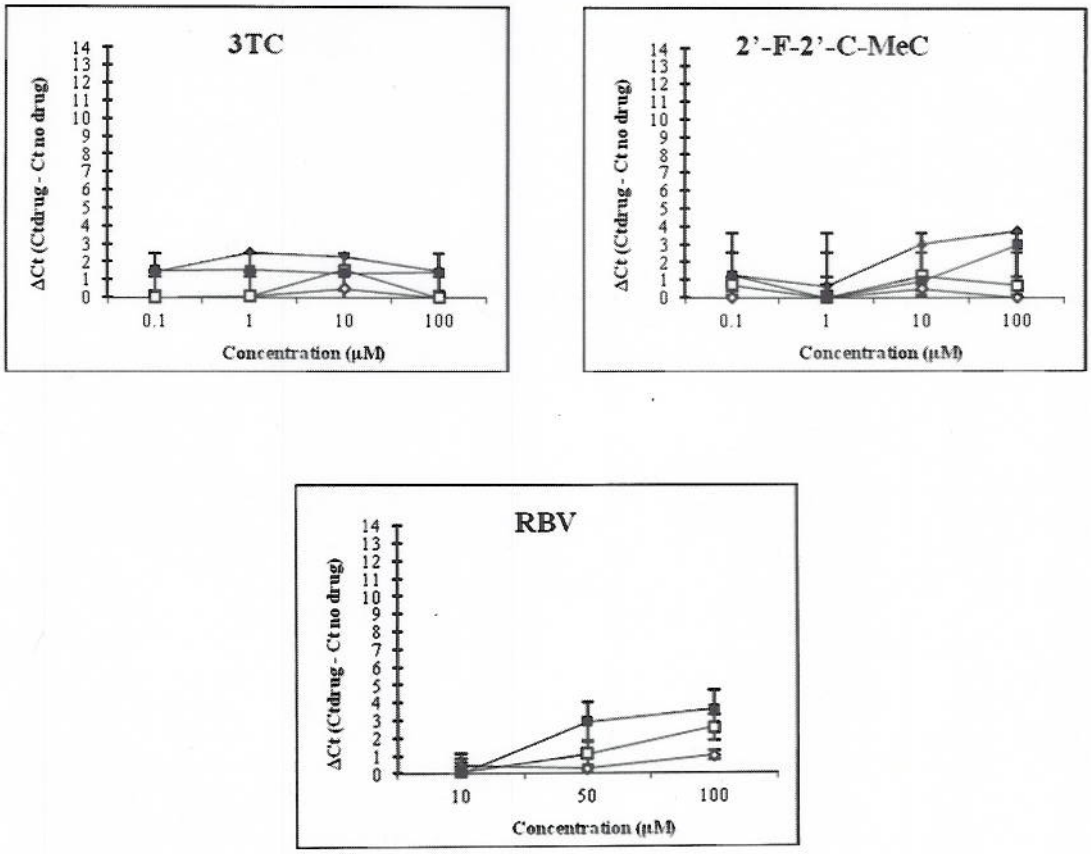
Supp. Figure 1: Single compound dose- and time-response curves for inhibition of MNV replication in RAW 264.7 cells. One-day-old semiconfluent RAW 264.7 cells were incubated with increasing concentrations (0.1 μM to 100 μM) of 3TC and NHC or increasing concentrations (10 μM to 200 μM) of RBV for 4 h, after which the media was removed and MNV was added to the cells. At (◇) 12 h, (□) 24 h, (■) 48 h, and (▲) 72 h post-treatment, MNV RNA levels were quantified by RT-qPCR. To express antiviral effectiveness, the mean Ct value from treated wells (Ct_{drug}) was subtracted from the mean Ct value of the no-drug control cells ($Ct_{no\ drug}$). A ΔCt of 3.3 equals 1-log reduction in NoV RNA levels (EC_{90}: 90% effective concentration). Each point represents the mean ± standard deviation of three replicate experiments (antiviral treatment) and 3 independent RT-qPCR runs.

Supplemental Figure 2



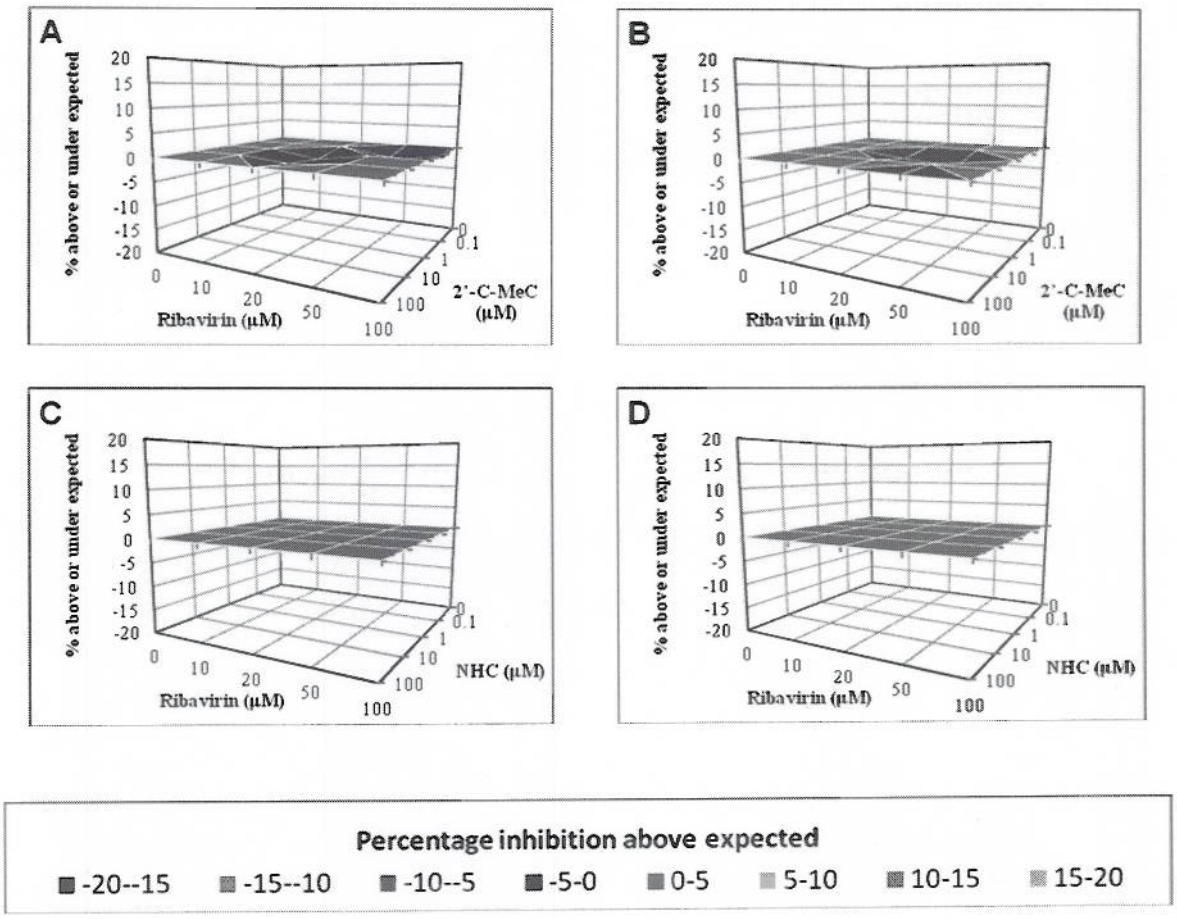
Supp. Figure 2: Reduction of MNV infectivity in RAW 264.7 cells by single compound treatment. One-day-old semiconfluent RAW 264.7 cells (24 wells) were incubated with increasing concentrations (0.1 μM to 100 μM) of 3TC and NHC or increasing concentrations (10 μM to 200 μM) of RBV for 4 h, after which the media was removed and MNV was added to the cells. At (□) 12 h, (■) 24 h, and (■) 48 h post-treatment, MNV infectivity was measured by $TCID_{50}$ assay. MNV titers for cells subject to antiviral treatment that were significantly reduced ($p < 0.05$) compared to the positive control (un-treated cells) are indicated (§) 12 h; (*) 24 h and (△) 48 h. Each point represents the mean ± standard deviation of 3 replicate experiments (antiviral treatment) and three independent $TCID_{50}$ assays.

Supplemental Figure 3



Supp. Figure 3: Single compound dose- and time-response curves for inhibition of NV replication in HG23 cells. One-day-old semiconfluent HG23 cells were incubated with increasing concentrations (0.1 μM to 100 μM) of 3TC and 2'-F-2'-C-MeC or RBV (10 to 100 μM). At (◇) 24 h, (□) 48 h, (■) 72 h, and (◆) 96 h post-treatment, medium was removed and NV RNA levels were quantified by RT-qPCR. To express antiviral effectiveness, the mean Ct value from treated wells (Ct_{drug}) was subtracted from the mean *Ct* value of the no-drug control cells ($Ct_{no\ drug}$). A ΔCt of 3.3 equals 1-log reduction in NoV RNA levels (EC_{90}: 90% effective concentration). Each point represents the mean ± standard deviation of 3 replicate experiments (antiviral treatment) and three independent RT-qPCR runs.

Supplemental Figure 4



Supp. Figure 4: Antiviral effect of the combination of RBV with 2'-C-MeC at, 72 h (A) and 96 h (B), or RBV with NHC at 72 h (C) and 96 h (D) in HG23 cells. Concentrations of each drug are indicated on the axes. Area above the zero plane on the z axis indicates doses of each drug that are synergistic, the zero plane indicates doses that are additive and the volume below indicates doses that are antagonistic. Data for the combinations are the mean value for five experiments (99% CI).